FDA Update

CLIAC Meeting
November 7, 2018

Peter Tobin, Ph.D.
Division of Program Operations and Management
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health
U.S. Food and Drug Administration

Today's Agenda:

- CDRH TPLC Reorganization & Staffing Changes
- Final Guidance Updates
- Breakthrough Device Program and FDA Innovation Challenges
- CLIA Waiver Updates

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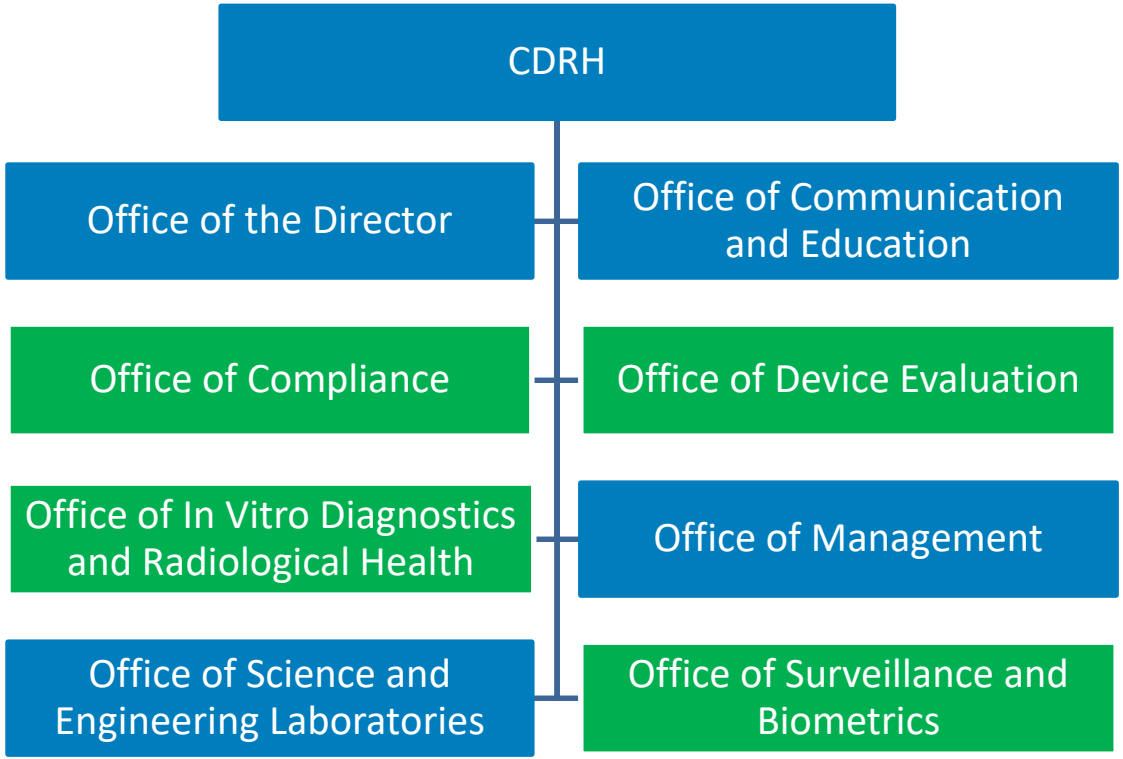
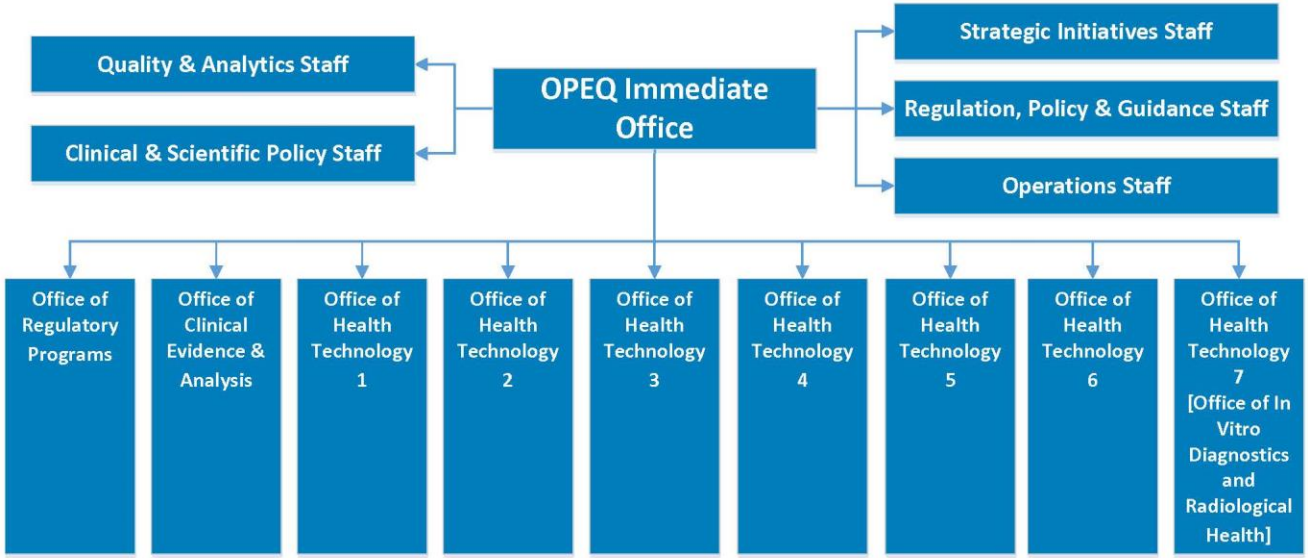
CDRH is reorganizing to support a Total Product Life Cycle (TPLC) approach



Future TPLC Super Office Design:

Office of Product Evaluation and Quality (OPEQ)



Introducing OIR's new Director, Tim Stenzel, MD, PhD

- **As a student,** studied microbiology and immunology at Duke, chemistry at Grinnell College
- **As an academic researcher,** created Duke's Clinical Molecular Diagnostics Laboratory and researched performance evaluation and quality assurance for genetic testing
- **As a developer,** created/launched numerous diagnostics, including NGS + CoDx
- **As an executive,** served in leadership roles at Invivoscribe, Quidel, Asuragen, Vysis/Abbott Molecular, and now FDA

Office of In Vitro Diagnostics and Radiological Health

Director	Timothy Stenzel
Deputy Dir. for New Product Evaluation	Donald St. Pierre
Deputy Dir. for Patient Safety and Product Quality	Scott Gonzalez (Acting)
Deputy Dir. for Personalized Medicine	Stayce Beck (Acting)
Deputy Dir. for Radiological Health	Robert Ochs
Associate Dir. for Programs and Performance	Elizabeth Hillebrenner
Associate Dir. for Strategic Initiatives	Toby Lowe
Associate Dir. for Regulatory Counsel	Scot McFarland
Chief Medical Officer	Vacant
Chief Medical Officer for Radiological Health	Donald L. Miller

Division of Chemistry and Toxicology Devices (DCTD)

Director – Courtney Lias
Deputy – Kellie Kelm

Division of Immunology and Hematology Devices (DIHD)

Director – Lea Carrington
Deputy – Vacant

Division of Microbiology Devices (DMD)

Director – Uwe Scherf
Deputy – Steve Gitterman

Division of Molecular Genetics and Pathology (DMGP)

Director – Reena Philip
Deputy – Yun-Fu Hu

Division of Mammography Quality Standards (DMQS)

Director – Helen Barr
Deputy – Preet Sudhaker

Division of Program Operations and Management (DPOM)

Director – Brendan O'Leary
Deputy – Vacant
PMO – Scott McCall

Division of Radiological Health (DRH)

Director – Thalia Mills (Acting)
Deputy – Michael O'Hara
Deputy – Ting Song (Acting)

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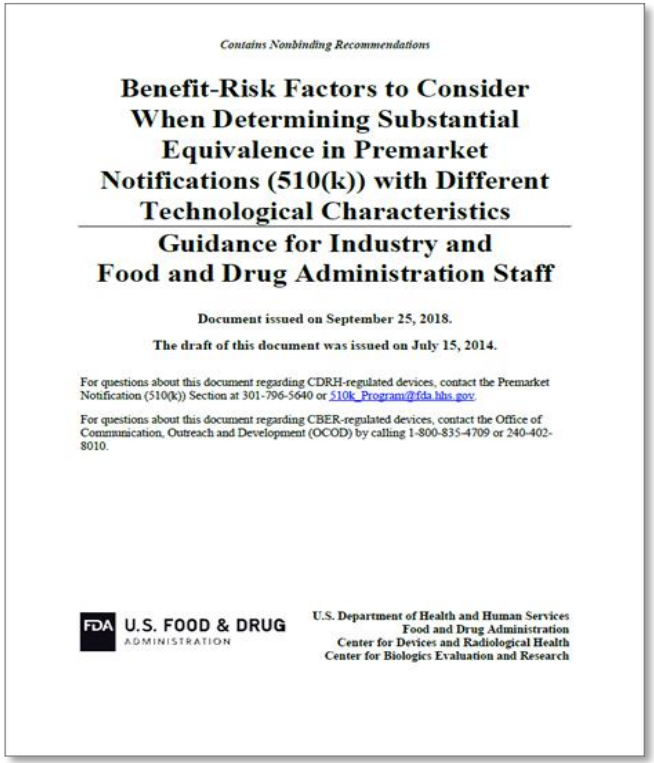
Final Guidances advance novel and risk-based regulatory approaches

1. Benefit-Risk for 510(k)
2. Voluntary Consensus Standards
3. LOINC Codes
4. NGS design, development and analytical validity
5. Genetic Variant Databases as sources of clinical evidence

New Benefit-Risk guidance is loaded with recommendations for diagnostics

For diagnostic devices specifically, benefit(s) in reference to the nature of the public health impact, could be based on a number of factors including:

- Identification of a specific disease;
- Provision of diagnosis at different stages of a disease;
- Prediction of future disease onset;
- Improvement of patient workflow;
- Increase in efficiency or examination;
- Provision of reproducible and quantifiable results contributing to the optimization of therapy and treatment; and
- Improvement of patient outcome (e.g., well-being, health status, safety of patients) by facilitating fewer missed diagnoses (or the right diagnosis the first time, hence the correct treatment plan) and/or identification of patients likely to respond to a given therapy and therefore enable treatment of the disease or reduce/prevent its spread, which can often be measured through the use of PROs.



Contains Nonbinding Recommendations

Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 25, 2018.

The draft of this document was issued on July 15, 2014.

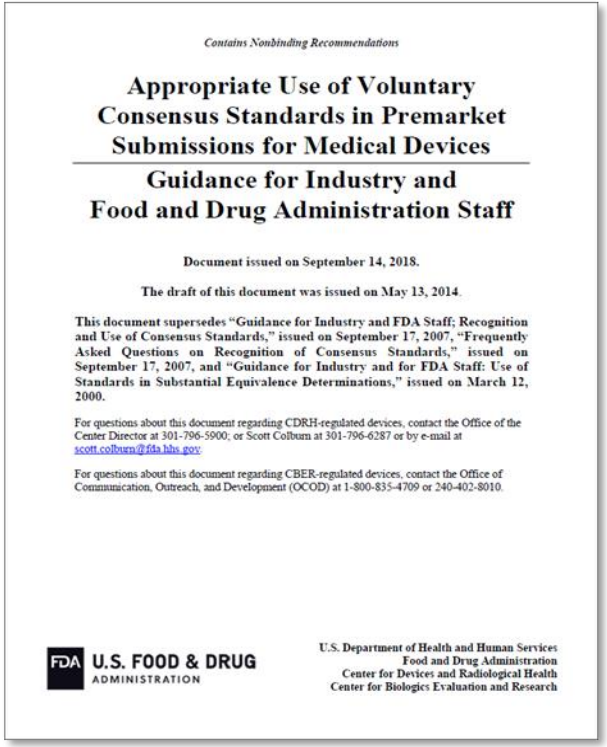
For questions about this document regarding CDRH-regulated devices, contact the Premarket Notification (510(k)) Section at 301-796-5640 or 510k_Program@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD) by calling 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

FDA continues increased emphasis on standards, implementing *Cures* legislation



Contains Nonbinding Recommendations

Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 14, 2018.

The draft of this document was issued on May 13, 2014.

This document supersedes "Guidance for Industry and FDA Staff; Recognition and Use of Consensus Standards," issued on September 17, 2007, "Frequently Asked Questions on Recognition of Consensus Standards," issued on September 17, 2007, and "Guidance for Industry and for FDA Staff: Use of Standards in Substantial Equivalence Determinations," issued on March 12, 2000.

For questions about this document regarding CDRH-regulated devices, contact the Office of the Center Director at 301-796-5900; or Scott Colburn at 301-796-6287 or by e-mail at scott.colburn@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

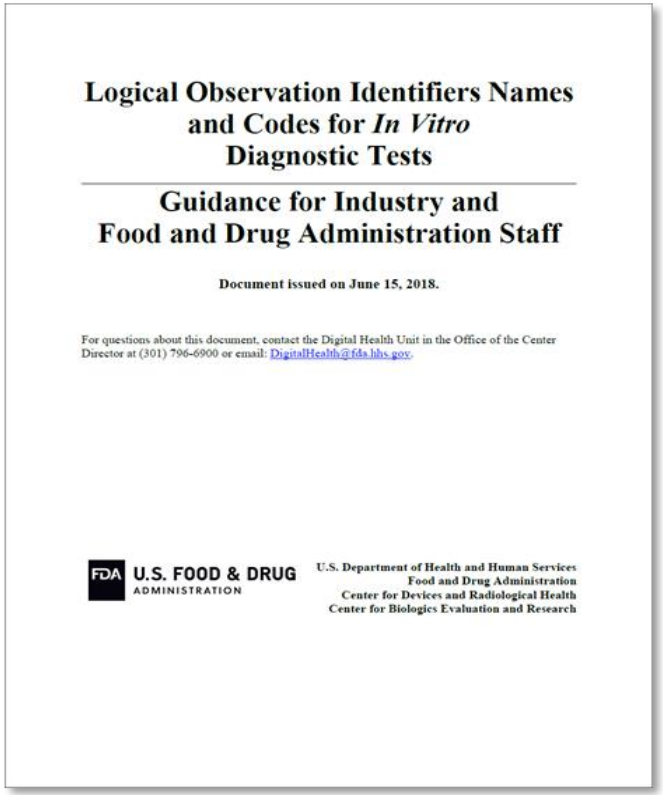
FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

"The use of consensus standards can increase predictability, streamline premarket review, provide clearer regulatory expectations, and facilitate market entry for safe and effective medical products."

We've clarified expectations for communicating LOINC codes for unapproved uses

- Upon receipt of an "…individual, unsolicited request…"
- "…where the manufacturer's response provides the appropriate LOINC coding…"
- "FDA does not intend to consider that response as evidence of the firm's intent that the product be used for unapproved or uncleared uses."*



Logical Observation Identifiers Names and Codes for *In Vitro* Diagnostic Tests

Guidance for Industry and Food and Drug Administration Staff

Document issued on June 15, 2018.

For questions about this document, contact the Digital Health Unit in the Office of the Center Director at (301) 796-6900 or email: DigitalHealth@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
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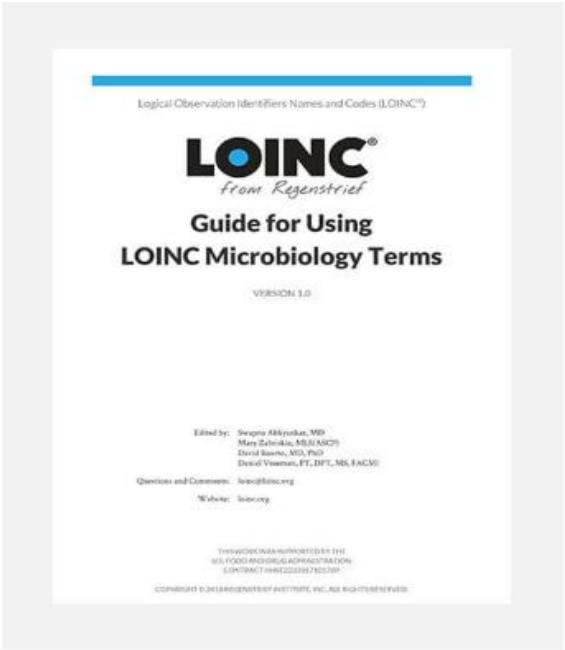
*** Read this guidance for full context. It's only 8 pages long.**

FDA supported the development of a new LOINC microbiology coding manual

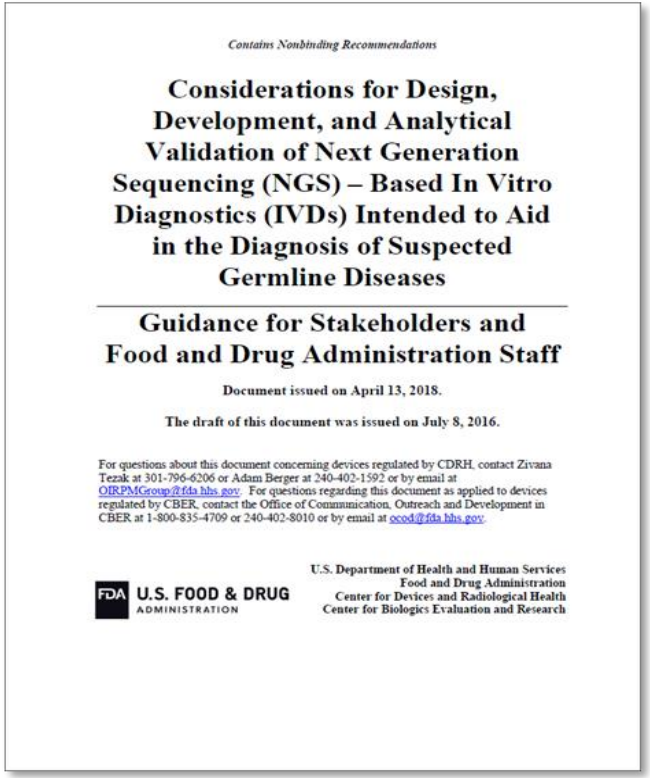


"Reducing inconsistency in reporting test results should substantially improve the reporting of antimicrobial resistance."

Scott Gottlieb, MD
FDA Commissioner

https://loinc.org/guides/micro

FDA believes innovative diagnostics merit innovative regulatory paradigms



Contains Nonbinding Recommendations

Considerations for Design, Development, and Analytical Validation of Next Generation Sequencing (NGS) – Based In Vitro Diagnostics (IVDs) Intended to Aid in the Diagnosis of Suspected Germline Diseases

Guidance for Stakeholders and Food and Drug Administration Staff

Document issued on April 13, 2018.

The draft of this document was issued on July 8, 2016.

For questions about this document concerning devices regulated by CDRH, contact Zivana Tezak at 301-796-6206 or Adam Berger at 240-402-1592 or by email at OIRPMGroup@fda.hhs.gov. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-8010 or by email at ocod@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

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Food and Drug Administration
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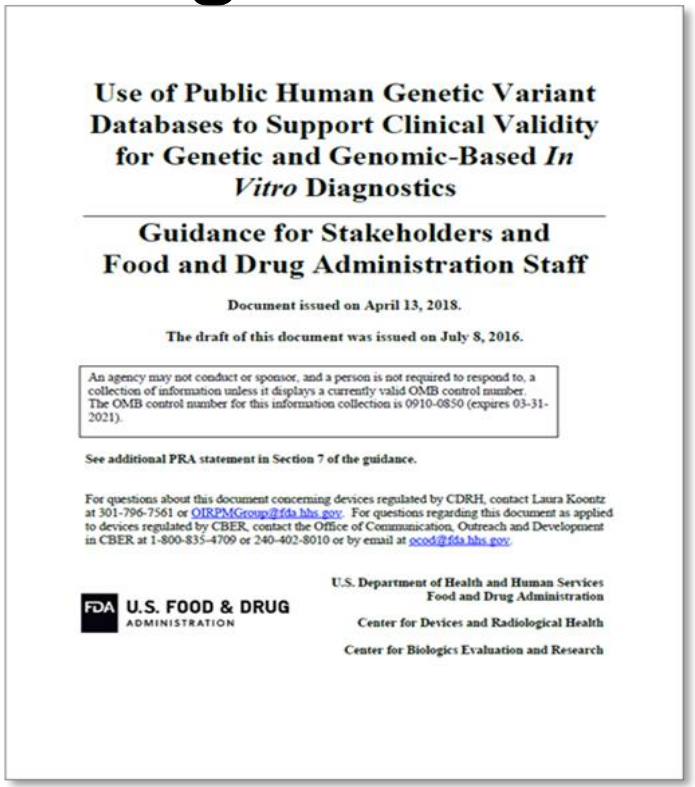
"FDA's vision is that NGS-based tests can be developed, validated, and offered for clinical use through a process that leverages appropriate standards, quality systems controls and community assessment of clinical validity to streamline the premarket review process."

Genetic Variant Database Guidance advances innovative paradigm for showing clinical validity

"publicly accessible databases of human genetic variants can serve as sources of valid scientific evidence to support the clinical validity of genotype-phenotype relationships"



Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based *In Vitro* Diagnostics

Guidance for Stakeholders and Food and Drug Administration Staff

Document issued on April 13, 2018.

The draft of this document was issued on July 8, 2016.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0850 (expires 03-31-2021).

See additional PRA statement in Section 7 of the guidance.

For questions about this document concerning devices regulated by CDRH, contact Laura Koontz at 301-796-7561 or OIRPMGroup@fda.hhs.gov. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-8010 or by email at ocod@fda.hhs.gov.

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More breakthrough diagnostics are coming to market through FDA

>95 designated devices

- **29** diagnostics

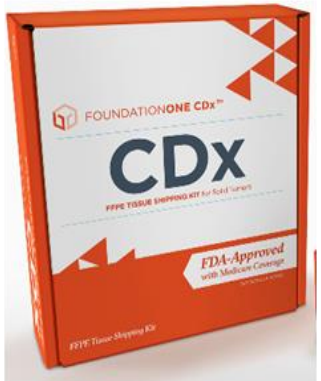
8 devices authorized to market

- **4** PMAs approved
- **2** 510(k)s cleared
- **2** De Novos granted

Data as of September 30, 2018

Early successes in breakthrough IVDs authorized to market include:

FoundationOne CDx



- 1st breakthrough to market
- 1st pan cancer CDx oncopanel

Banyan Brain Trauma Indicator

1st breakthrough De Novo to market

1st Blood test for TBI

More to come….

FDA launched an innovation challenge for devices to prevent and treat opioid use disorder

Applicants selected will Work directly with FDA to accelerate development of innovative devices to help combat the opioid crisis

https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhinnovation/ucm609082.htm

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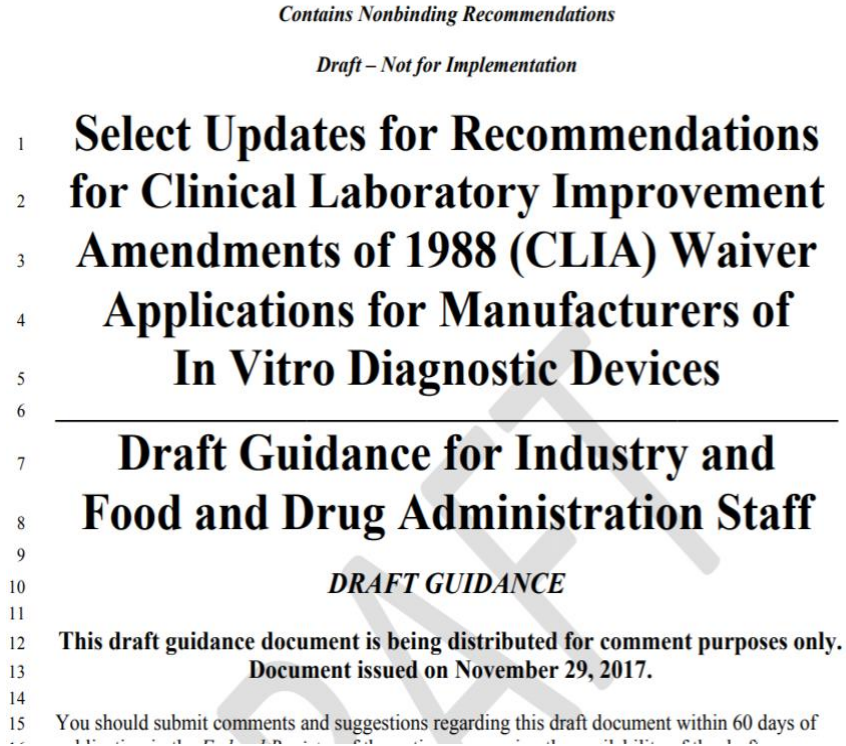
We're reissuing revised CLIA Waiver guidances in draft before finalizing



Contains Nonbinding Recommendations

Draft – Not for Implementation

Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices

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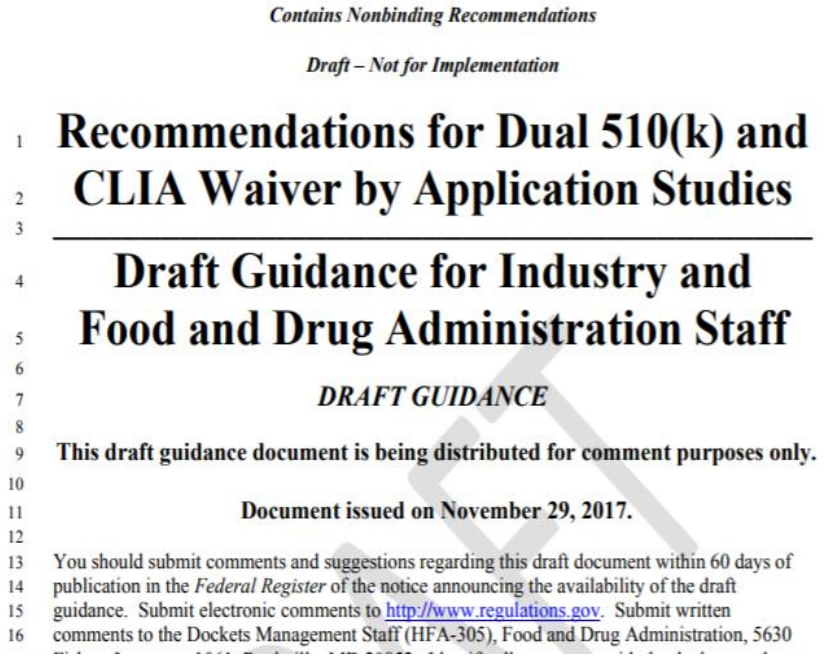
Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.
Document issued on November 29, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of



Contains Nonbinding Recommendations

Draft – Not for Implementation

Recommendations for Dual 510(k) and CLIA Waiver by Application Studies

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Draft Guidance for Industry and Food and Drug Administration Staff

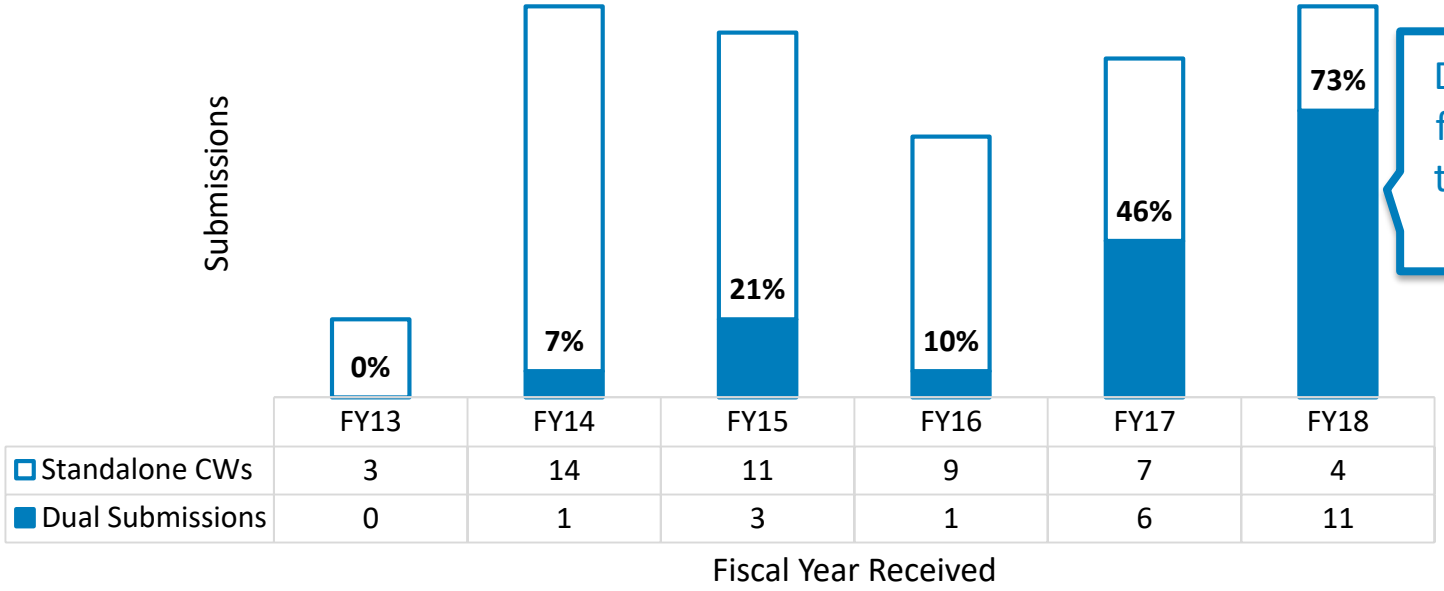
DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on November 29, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630

Dual CWs eclipsed standalone CWs as the preferred waiver pathway in FY18



	FY13	FY14	FY15	FY16	FY17	FY18
Standalone CWs	3	14	11	9	7	4
Dual Submissions	0	1	3	1	6	11

CLIA Waiver (CW) Decision Summaries:
https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm578178.htm

Questions?

CLIA@fda.hhs.gov